REMARKS

By the amendment to Claim 2, the claims have been amended to address the Board's concern that the present compositions are administered to the same subject population as those in the cited references. In the amended claims the subjects targeted for the present claimed method are specified as those having or at risk for systemic diseases induced by the presence of pathogens in the oral cavity. Claim 2 is further amended to specify in the body of the claim that the H2-antagonist is present in an amount effective to mediate systemic host reaction to the presence of periodontal pathogens in the subject's oral cavity and to reduce risk factors for systemic disease, thereby promoting whole body or systemic health.

Claims 2-4 and 7 have been rejected as being anticipated by Pan et al. (WO 97/16159) and by Singer et al. (US 5,364,616). Claim 2 is rejected as being anticipated by Tsujita et al, (JP 04089428A). It is contended that the presently claimed whole body health benefits are inherent in the referenced methods.

It is respectfully submitted that the claims as now presented are novel over the prior art.

As now specified, the patients targeted for the presently claimed method are subjects who are at risk for the development of one or more of systemic conditions induced by oral cavity pathogens. These conditions include heart disease, stroke, diabetes, severe respiratory infections, delivery of premature or low birth weight infants, and post-partum dysfunction in neurologic and developmental functions. In contrast, the subjects intended in the referenced methods are those in need of treatment or prevention of non-systemic or localized conditions in the mouth such as plaque, gingivitis and periodontal disease.

The present claims are directed to a process namely topical administration to the oral cavity of a composition comprising a H-2 antagonist, having a new or second medicinal use, specifically mediating systemic host reaction to the presence of periodontal pathogens in the subject's oral cavity and thereby preventing development of certain systemic diseases and promoting whole body health in a specified group of subjects.

Applicants submit there is no evidence in the record to support the Examiner's and

Board's finding that the referenced methods inherently anticipate the claimed invention of Claims 2 to 4 and 7. A finding of inherency requires that practicing the prior art method would necessarily and inevitably result in the claimed invention, *i.e.*, promotion of whole body health. Inherent anticipation must be established by more than mere probabilities or possibilities. In order for a prior art reference to amount to an inherent anticipation of a claim, all the elements of the claim must *necessarily, inevitably* and *always* result from the prior art disclosure; mere possibilities or probabilities are not sufficient. *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981), citing *Hansgirg v. Kemmer*, 102 F.2d 212, 214, 40 U.S.P.Q. 665, 667 (C.C.P.A. 1939). "The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient." *Rapoport v. Dement* 254 F.3d 1053, 1063 (Fed Cir. 2001), citing *Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir.1991) (emphasis in original). Furthermore, an accidental or unwitting duplication of an invention may not constitute an anticipation. *In re Marshall*, 578 F.2d 301, 304 (Fed Cir. 1978). Thus, in order for Pan, Singer or Tsujita to inherently anticipate the claimed invention, the method described must result in the claimed invention, *i.e.*, promotion of whole body health, *each time and every time* the prior art methods are practiced. Given the vagaries of how the prior art methods may be practiced, inherent anticipation of the claimed method has not been established in this record.

In *Marshall* (Id.), the US Court of Customs and Patent Appeals reversed the rejection of Marshall's claims on the grounds of anticipation because no single piece of prior art contained all the material elements of the claims and because the claims described a new and unanticipated use for an existing drug. Marshall's claims were directed to a process for controlling weight using an anesthetic drug, oxethazaine, to inhibit release of the pancreatic secretory hormones, secretin and pancreozymin, in order to control weight. The applied art was the *Physician's Desk Reference* (PDR), which taught using drugs containing the anesthetic oxethazaine to inhibit release of the acid-stimulating hormone, gastrin, in order to treat esophagitis, gastritis, peptic ulcer and irritable colon syndrome. There was no disclosure in the PDR of the activity of oxethazaine to inhibit release of the secretory

hormones, which activity makes it useful for losing weight. Therefore if a subject ever lost weight by following the PDR teachings it was an unrecognized accident. The CCPA stated:

> *An accidental or unwitting duplication of an invention cannot constitute an anticipation. In re Felton, 484 F.2d 495, 500, 179 USPQ 295, 298 (CCPA 1973).*

As in *Marshall*, the applied citations do not disclose the newly discovered activity of H2-antagonists when topically administered to the oral cavity, specifically increasing the barrier function of the gingival tissues and decreasing the blood levels of C-reactive protein and apolipoprotein B, such activity preventing the development of systemic disease and therefore promoting whole body health in subjects having or at risk for systemic diseases associated with increased levels of C-reactive protein and apolipoprotein B. There is no recognition in the cited art of such patient population and even less that the present claimed treatment would benefit such patient population. If practicing the referenced methods decreased the blood levels and C-reactive protein and apolipoprotein B and thereby reduced risk factors for heart disease and promoted systemic health, it would be an accidental duplication of the present invention. It is respectfully submitted that the applied citations do not constitute an anticipation of the present invention.

The Examiner correctly noted that the *Shetty* case previously cited by Applicants was concerned with a 103 rejection. *Shetty* is cited because of its relevance to the issue of inherency as it relates to biological or medicinal activity of chemicals and compositions and methods of use thereof. Case law supports the proposition that in the field of biological or medicinal inventions, inherency of the medicinal activity is not the material issue. Rather, it is whether or not such medicinal activity would have been recognized by those skilled in the art and applied to a new or second medicinal "use". There is lack of predictability of useful new results from simply the chemical structure of drug substances and their known activity.

It is further submit that a *prima facie* case of inherency has not been established as required under MPEP 2112 and 2131.02 Section III. As stated therein:

"In relying upon the theory of inherency, the examiner must provide a basis in fact and or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art."

"The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish that result or characteristic."

To support the finding of inherency, the Examiner reasons that the presently claimed new use of promoting systemic health is a direct result of the antimicrobial mechanism of action of the referenced methods and that one of ordinary skill in the art would recognize that the referenced methods would reduce the quantity of oral pathogens in the oral cavity and that this in turn would reduce the quantity of pathogens entering the bloodstream from the gums and that reduction of said pathogens in the blood would promote systemic or whole body health.

It is respectfully submitted that such conclusion of inherency is based upon improper hindsight reasoning. There is absolutely no teaching in the referenced art relating to the possibility that pathogens in the mouth and bacterial toxins could enter the systemic circulation via the gums, that such entry would prompt systemic inflammatory mechanisms and complications, i.e., increase blood levels of C-reatcive protein and apolipoprotein B, that such events would be risk factors for development of systemic diseases and that such risk factors and systemic diseases would be decreased by topically administering a H2-antagonist. As established in the record from the declaration by present inventor Robert E. Singer, Jr. (submitted in the response dated June 24, 2002 to the Office Action dated December 27, 2001), topical treatment of oral tissues with H2 antagonists serves to increase the barrier function of gingival tissues. The series of studies conducted under Mr. Singer's direction demonstrated that topical H2 antagonists enhance the barrier or protective function of gingival tissues thereby preventing oral pathogens and their products from entering into the systemic circulation. Topical administration of H2 antagonist compositions to the oral cavity further serves to decrease the blood levels of C-reactive protein and apolipoprotein B,

thereby preventing development of certain systemic diseases and promoting systemic or whole body health.

The referenced art teach nothing more than that H2 antagonists are useful in treating and preventing inflammations in the oral cavity such as gingivitis and periodontitis. Nothing is said in the references that oral pathogens and toxins could pose a risk to systemic health if entry into the systemic circulation occurred, much less that H2-antagonists would enhance the barrier or protective function of gingival tissues and prevent such entry and even less that topically applied H2-antagonists would decrease the blood levels of C-reactive protein and apolipoprotein B. Without the benefit of the present disclosure, it would not be recognized that topical administration of H2-antagonists would have such biological activity and be effective to promote systemic or whole body health by reducing risk factors for the development of particular systemic diseases.

In light of the amendments and remarks above, Applicants submit that the pending claims are allowable. Applicants respectfully request that the above amendments and remarks be made of record in the instant application.

Respectfully submitted,
THE PROCTER & GAMBLE COMPANY

By 
Emelyn L. Hiland
Agent for Applicant(s)
Registration No. 41,501
(513) 622-3236

May 24, 2006
Customer No. 27752